PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See item 4 below |
|---|---|---|
| International application No<br>PCT/IB2006/003511 | International filing date (*day/month/year*)<br>27 September 2006 (27.09.2006) | Priority date (*day/month/year*)<br>28 September 2005 (28.09.2005) |
| International Patent Classification (IPC) (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 | | |
| Applicant<br>AURIS MEDICAL AG | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis* 1(a).

2. This REPORT consists of a total of 12 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

   - [X] Box No. I — Basis of the report
   - [X] Box No. II — Priority
   - [X] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - [X] Box No. IV — Lack of unity of invention
   - [X] Box No. V — Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - [X] Box No. VI — Certain documents cited
   - [ ] Box No. VII — Certain defects in the international application
   - [ ] Box No. VIII — Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

| | Date of issuance of this report<br>02 April 2008 (02.04.2008) |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No. +41 22 338 82 70 | Authorized officer<br>Cecile Chatel<br>e-mail: pt13.pct@wipo.int |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
*(day/month/year)* see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

**FOR FURTHER ACTION**
See paragraph 2 below

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/IB2006/003511 | 27.09.2006 | 28.09.2005 |

International Patent Classification (IPC) or both national classification and IPC
INV. A61K31/00 A61K31/135 A61K31/517 A61K31/439 A61K31/662 A61K31/4535 A61P27/16 A61K49/00

Applicant
AURIS MEDICAL AG

1. This opinion contains indications relating to the following items:

   - ☒ Box No. I Basis of the opinion
   - ☒ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☒ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 43*bis* 1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☒ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

   If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

   If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

   For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA: | Date of completion of this opinion | Authorized Officer |
|---|---|---|
| European Patent Office - P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040 Tx. 31 651 epo nl<br>Fax: +31 70 340 - 3016 | See form PCT/ISA/210 | Hoff, Philippe<br>Telephone No. +31 70 340-3520 |

Form (PCT/ISA/237) (Cover Sheet) (April 2005)

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

**Box No. II Priority**

1. ☐ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☒ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-9 (with respect to industrial applicability), 10-21

because:

☒ the said international application, or the said claims Nos. 1-9 (with respect to industrial applicability) relate to the following subject matter which does not require an international search *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for the whole application or for said claims Nos. 10-21

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details

**Box No. IV Lack of unity of invention**

1. ☑ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:

   ☐ paid additional fees

   ☐ paid additional fees under protest and, where applicable, the protest fee

   ☐ paid additional fees under protest but the applicable protest fee was not paid

   ☒ not paid additional fees

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   **see separate sheet**

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-9

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | |
| | No: | Claims | 1-9 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-9 |
| Industrial applicability (IA) | Yes: | Claims | |
| | No: | Claims | 1-9 (see separate sheet) |

2. Citations and explanations

**see separate sheet**

**Box No. VI Certain documents cited**

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

**Re Item II.**

Earlier International Application WO-A-2005/094799 (D1) published on 13.10.2005 has the filing date of 29.03.2005. It discloses a method for treating or preventing tinnitus induced by cochlear excitotoxicity in a human, the method comprising administering an N-methyl-D-aspartate (NMDA) receptor antagonist to suppress, reduce or prevent NMDA receptor mediated aberrant activity of the auditory nerve.
The application US 11/236,941 (date of filing 28.09.2005) to which the priority claim of the present invention is directed is therefore not the application disclosing for the **first time** a part of the subject-matter of the present International Application.
As the subject-matter as described above was disclosed in a still earlier application (D1) originating from the same applicant (Auris Medical AG), the application US 11/236,941 is in fact not the "first application" in sense of Article 8 PCT. Therefore the priority claim is invalid for the subject-matter already disclosed in the still earlier application D1 (namely the subject-matter of present claims 1-9) and the document D1 will be considered as forming part of the state of the art within the meaning of Rule 64.1 PCT.

**Re Item III.**

1. Claims 1-9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

2. In reply to the objection to lack of unity, the applicant has not paid additional search fees. The international search report has been established for the first invention only.

**No opinion will be given in respect of subject-matter which is not covered by the search report (Rule 66.1(e) PCT).**

**Re Item IV.**

The separate inventions/groups of inventions are:

1. Claims: 1-9
Method for treating tinnitus induced by cochlear excitotoxicity comprising administering an NMDA antagonist

2. Claims: 10-21
An electrophysical method for identifying compounds effective in the treatment of tinnitus

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

The problems to be solved by the present invention are:

1. to provide medicaments for the treatment of tinnitus

2. to provide a new method for the screening of compounds effective in the treatment of tinnitus

The proposed solutions are:

a. for problem 1: the use of an NMDA receptor antagonist

b. for problem 2: the method such as defined in claims 10 and 18 and which include the measure of the ensemble spontaneous activity (ESA) of the ear after administration of the test substance, preferably an NMDA receptor antagonist

Rule 13.1 PCT requires a common inventive concept between a group of inventions

claimed in an international patent application. This means that there must be either a common technical problem or at least, if there is more than one technical problem (as in the present case), there must be one single technical concept behind the solutions of these different problems.

The only single technical concept behind the solutions of the different problems 1 and 2 posed above is the NMDA receptor-mediated aberrant activity of the auditory nerve in tinnitus induced by cochlear excitotoxicity and its treatment with NMDA receptor antagonist.

However, the use of NMDA receptor antagonists to suppress excessive NMDA receptor-mediated signals in tinnitus induced by cochlear excitotoxicity is known in the state of the art.

The document WO 2004/022069 discloses the use of NMDA antagonists (7-chlorokynurenate, D-AP5, MK-801, gacyclidine) for treating an inner ear disorder caused by aberrant glutamate-mediated neurotransmission such as tinnitus.

The use of NMDA antagonists (7-chlorokynurenate, MK-801, gacyclidine) for treating tinnitus by topical administration via the round window membrane to the inner ear is also disclosed in XP8054642, XP8054725 and XP8054645.

Consequently, because the use of NMDA receptor antagonists in the treatment of tinnitus has been already described in the prior art, there is no single general inventive concept linking the treatment of tinnitus with an NMDA receptor antagonist and the method for the screening of compounds (in particular NMDA antagonists) for the treatment of tinnitus.

In the present application no further technical feature(s) can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Consequently, the present application lacks unity of invention, and the different solutions not belonging to a common inventive concept are identified as the different subjects listed above. Each of the inventions listed is a distinct invention.

characterised by its own special technical feature, defining the contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

As the applicant has not had a search report drawn up on the other inventions, the present opinion will be established on the basis of the invention in respect of which a search has been carried out, in other words the first invention.

**Re Item V.**

Reference is made to the following documents:

D1: WO 2005/094799 A (AURIS MEDICAL AG [CH]; INST NAT SANTE RECH MED [FR]; GUITTON MATTHIEU) 13 October 2005 (2005-10-13)
D2: GUITTON MATTHIEU J ET AL: "New pharmacological strategies to restore hearing and treat tinnitus." ACTA OTO-LARYNGOLOGICA. MAY 2004, vol. 124, no. 4, May 2004 (2004-05), pages 411-415, XP008054645 ISSN: 0001-6489
D3: WO 2004/022069 A (DURECT CORPORATION; PUEL, JEAN-LUC; PUJOL, REMY; CHRISTEN, YVES) 18 March 2004 (2004-03-18)
D4: GUITTON MATTHIEU J ET AL: "Salicylate induces tinnitus through activation of cochlear NMDA receptors." JOURNAL OF NEUROSCIENCE, vol. 23, no. 9, 1 May 2003 (2003-05-01), pages 3944-3952, XP008054642 ISSN: 0270-6474 cited in the application
D5: GUITTON M J ET AL: "Cochlear NMDA receptors and tinnitus" AUDIOLOGICAL MEDICINE 2004 UNITED KINGDOM, vol. 2, no. 1, March 2004 (2004-03), pages 3-7, XP008054725 ISSN: 1651-386X
D6: PUEL JEAN-LUC ET AL: "[Treatment of tinnitus. New perspectives]" PRESSE MEDICALE (PARIS, FRANCE : 1983) 13 JUL 2002, vol. 31, no. 24, 13 July 2002 (2002-07-13), pages 1137-1143, XP008054746 ISSN: 0755-4982
D7: SIMPSON J J ET AL: "Recent advances in the pharmacological treatment of tinnitus" TRENDS IN PHARMACOLOGICAL SCIENCES 1999 UNITED KINGDOM, vol. 20, no. 1, 1999, pages 12-18, XP008054690 ISSN: 0165-6147
D8: US-A-6 066 652 (ZENNER ET AL) 23 May 2000 (2000-05-23) cited in the application
D9: US-A-5 716 961 (SANDS ET AL) 10 February 1998 (1998-02-10) cited in the

application

2 NOVELTY (Article 33(2) PCT)

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-9 is not new in the sense of Article 33(2) PCT.
Document D1 (examples; claims) discloses a method for treating or preventing tinnitus induced by cochlear excitotoxicity in a human, the method comprising administering a composition comprising an NMDA receptor antagonist to suppress, reduce or prevent NMDA receptor mediated aberrant activity of the auditory nerve.
The NMDA receptor antagonists disclosed are ketamine, 7-chlorokynurenate, D-2-amino-5-phosphonopentanoic acid (D-AP5), dizocilpine (MK 801) and gacyclidine.
The composition is administered topically or locally via the round or oval window membrane to the inner ear or administered topically or locally by device of invasive drug delivery techniques to the inner ear.

2.2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-9 is not new in the sense of Article 33(2) PCT.
The documents D2 to D5 disclose the use of NMDA antagonists (7-chlorokynurenate, D-AP5, MK-801, gacyclidine) for treating tinnitus by topical administration via the round window membrane to the inner ear.

2.3 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1,2,4,7-9 is not new in the sense of Article 33(2) PCT.
The documents D6,D7,D8,D9 disclose the use of various NMDA receptor antagonists for treating tinnitus (see the corresponding passages cited in the search report).

3 INVENTIVE STEP (Article 33(3) PCT)

3.1 Should the Applicant have overcome the objections of lack of novelty raised above, an inventive step could not be acknowledged over D1 to D9 as the present subject-matter of claims 1-9, as far as novel, appears to be an obvious alternative over said documents (Article 33(3) PCT).
NMDA antagonists have been already described in the prior art as being useful in the treatment of tinnitus.

4 INDUSTRIAL APPLICABILITY (Article 33(4) PCT)

4.1 For the assessment of the present claims 1-9 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**Re Item VI.**

Since the priority claim is invalid for the subject-matter of present claims 1-9, the document D1 has been considered as forming part of the state of the art within the meaning of Rule 64.1 PCT for said subject-matter (see also section II above).

# INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2006/003511

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/00 A61K31/135 A61K31/517 A61K31/439 A61K31/662
A61K31/4535 A61P27/16 A61K49/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, SCISEARCH, CHEM ABS Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | GUITTON MATTHIEU J ET AL: "m-Chlorophenylpiperazine exacerbates perception of salicylate-induced tinnitus in rats." THE EUROPEAN JOURNAL OF NEUROSCIENCE NOV 2005, vol. 22, no. 10, November 2005 (2005-11), pages 2675-2678, XP002452890 ISSN: 0953-816X the whole document | 1-9 |
| P,X | WO 2005/094799 A (AURIS MEDICAL AG [CH]; INST NAT SANTE RECH MED [FR]; GUITTON MATTHIEU) 13 October 2005 (2005-10-13) abstract; claims; examples | 1-9 |

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 28 September 2007 | 15/01/2008 |

| Name and mailing address of the ISA/ | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx 31 651 epo nl,<br>Fax: (+31-70) 340-3016 | Hoff, Philippe |

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | GUITTON MATTHIEU J ET AL: "New pharmacological strategies to restore hearing and treat tinnitus." ACTA OTO-LARYNGOLOGICA. MAY 2004, vol. 124, no. 4, May 2004 (2004-05), pages 411-415, XP008054645 ISSN: 0001-6489 the whole document | 1-9 |
| X | WO 2004/022069 A (DURECT CORPORATION; PUEL, JEAN-LUC; PUJOL, REMY; CHRISTEN, YVES) 18 March 2004 (2004-03-18) page 1, line 1 - line 16 page 3, line 15 - page 4, line 13 page 12, line 8 - line 16 page 14, line 5 - page 16, line 10; claims; examples | 1-9 |
| X | GUITTON MATTHIEU J ET AL: "Salicylate induces tinnitus through activation of cochlear NMDA receptors." JOURNAL OF NEUROSCIENCE, vol. 23, no. 9, 1 May 2003 (2003-05-01), pages 3944-3952, XP008054642 ISSN: 0270-6474 cited in the application the whole document | 1-9 |
| X | GUITTON M J ET AL: "Cochlear NMDA receptors and tinnitus" AUDIOLOGICAL MEDICINE 2004 UNITED KINGDOM, vol. 2, no. 1, March 2004 (2004-03), pages 3-7, XP008054725 ISSN: 1651-386X the whole document | 1-9 |
| X | PUEL JEAN-LUC ET AL: "[Treatment of tinnitus. New perspectives]" PRESSE MEDICALE (PARIS, FRANCE : 1983) 13 JUL 2002, vol. 31, no. 24, 13 July 2002 (2002-07-13), pages 1137-1143, XP008054746 ISSN: 0755-4982 abstract page 1140, left-hand column, paragraph 2 - page 1141, left-hand column, paragraph 1 | 1,2,4-9 |

-/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | SIMPSON J J ET AL: "Recent advances in the pharmacological treatment of tinnitus" TRENDS IN PHARMACOLOGICAL SCIENCES 1999 UNITED KINGDOM, vol. 20, no. 1, 1999, pages 12-18, XP008054690 ISSN: 0165-6147 page 15, right-hand column, last paragraph - page 17, right-hand column, last paragraph; table 1 | 1,2,4-9 |
| X | US 6 066 652 A (ZENNER ET AL) 23 May 2000 (2000-05-23) cited in the application the whole document | 1,2,4-9 |
| X | US 5 716 961 A (SANDS ET AL) 10 February 1998 (1998-02-10) cited in the application column 1, line 37 - line 67; claims | 1,2,4-9 |
| A | KALTENBACH J A ET AL: "Plasticity of spontaneous neural activity in the dorsal cochlear nucleus after intense sound exposure" HEARING RESEARCH 2000 NETHERLANDS, vol. 147, no. 1-2, 2000, pages 282-292, XP008054667 ISSN: 0378-5955 page 288, right-hand column, paragraph 1 page 290, left-hand column, paragraph 2 - right-hand column, paragraph 1 | 1-9 |
| A | KENMOCHI M ET AL: "Salicylate and quinine affect the central nervous system" HEARING RESEARCH 1997 NETHERLANDS, vol. 113, no. 1-2, 1997, pages 110-116, XP008054659 ISSN: 0378-5955 page 114, left-hand column, paragraph 3 - right-hand column, paragraph 1 | 1-9 |

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2006/003511

**Box No. II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box No. III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-9

Method for treating tinnitus induced by cochlear excitotoxicity comprising administering an NMDA antagonist

2. claims: 10-21

An electrophysical method for identifying compounds effective in the treatment of tinnitus

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2006/003511

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 2005094799 A | 13-10-2005 | AU 2005229543 A1 | 13-10-2005 |
| | | BR PI0508251 A | 31-07-2007 |
| | | CA 2558896 A1 | 13-10-2005 |
| | | CN 1972677 A | 30-05-2007 |
| | | EP 1729753 A2 | 13-12-2006 |
| | | JP 2007530622 T | 01-11-2007 |
| | | US 2006063802 A1 | 23-03-2006 |
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(71) Applicants *(for all designated States except US)*: **AURIS MEDICAL AG** [CH/CH]; Rueffelcfstrasse 1, CH-4573 Lohn-Ammannsegg (CH). **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE** [FR/FR]; 101, rue de Tolbiac, F-75654 Paris Cedex 13 (FR).

(72) Inventors: **GUTTON, Matthieu**, 62, rue P. Picasso, F-76770 Le Houlme (FR). **PUEL, Jean-Luc**; Plan de Milouin, Lot Le Ramasol, F-34660 Cournonterral (FR). **PUJOL, Remy**, 213, Avenue du Père Soulas, F-34090 Montpellier (FR). **RUEL, Jerome**; 2448 avenue du Pere Soulas, F-34090 Montpellier (FR). **WANG, Jing**, 12, rue des Bonnes Gens, F-34400 Lunel (FR).

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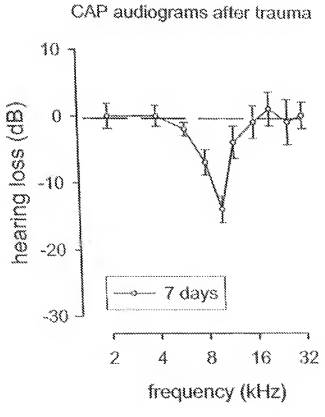
(54) Title: USE OF AN NMDA RECEPTOR ANTAGONIST THE TREATMENT OF TINNITUS INDUCED BY COCHLEAR EXCITOTOXICITY




(57) Abstract: The invention relates to methods for the prevention and/or treatment of tinnitus induced by cochlear excitotoxicity. In these methods, a pharmaceutical composition comprising an NMDA receptor antagonist is administered to an individual in need of such treatment by appropriate devices and/or formulations for local administration to the inner ear. The tinnitus to be prevented and/or treated may be provoked by acoustic trauma, presbycusis, ischemia, anoxia, treatment with one or more ototoxic medications, sudden deafness, or other cochlear excitotoxic-inducing occurrence. The invention also relates to method for the identification of compounds effective in the treatment and prevention of tinnitus by a novel screening method incorporating an electrophysiological test method.

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